

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

HARRISON GODDARD FOOTE
Tower House
Merrion Way
Leeds LS2 8PA
GRANDE BRETAGNE

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing
(day/month/year)

05.04.2001

Applicant's or agent's file reference
LPB/P15578WO

IMPORTANT NOTIFICATION

International application No.
PCT/GB99/04141

International filing date (day/month/year)
14/12/1999

Priority date (day/month/year)
15/12/1998

Applicant

THE UNIVERSITY OF YORK et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.


4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

 European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Zoglauer, H

Tel. +49 89 2399-8051





PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference LPB/P15578WO		FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB99/04141	International filing date (day/month/year) 14/12/1999	Priority date (day/month/year) 15/12/1998	
International Patent Classification (IPC) or national classification and IPC C12N15/82			
Applicant THE UNIVERSITY OF YORK et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 2 sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none">I <input checked="" type="checkbox"/> Basis of the reportII <input type="checkbox"/> PriorityIII <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicabilityIV <input type="checkbox"/> Lack of unity of inventionV <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statementVI <input type="checkbox"/> Certain documents citedVII <input type="checkbox"/> Certain defects in the international applicationVIII <input checked="" type="checkbox"/> Certain observations on the international application			
Date of submission of the demand 12/07/2000		Date of completion of this report 05.04.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel: +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Burkhardt, P Telephone No. +49 89 2399 7456	

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/04

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-32 as originally filed

Claims, No.:

1-14 with telefax of 22/12/2000

Drawings, sheets:

1/17-17/17 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure of the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/04

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 1 - 9, 12
	No: Claims 10, 11, 13, 14
Inventive step (IS)	Yes: Claims 1 - 5, 8, 9, 12
	No: Claims 6, 7
Industrial applicability (IA)	Yes: Claims 1 - 14
	No: Claims

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No.: PCT/GB99/04141

Re Item I

Basis of the opinion

The amended claims filed with the letter of 22.12.2000 are formally acceptable under Article 34(2)(b) PCT.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following documents (D) are referred to in this report; the numbering is following the order of the International Search Report:

- D1 Crofts *et al.*, 1998. Plant Cell 10:813-823.
- D2 Coleman *et al.*, 1997. PNAS USA 94:7094-7097.

1. Interpretation of claims

1.1 In order to allow a meaningful examination of the present set of claims it was assumed that the methods relate to transgenic plants that have been transformed with a nucleic acid sequence encoding a luminal binding protein (BiP).

1.2 Please also note the comments in section VIII.

2. Article 33(2)(3) PCT (Novelty and inventive step)

2.1 Present claim 1 is directed to a method of reducing the period within which a plant's natural defence mechanism responds to pathogen attack by over expression of BiP. The transgenic plants disclosed in D1 and D2 have been created in the same way as those of the present invention. The result to be achieved, namely to obtain an improved pathogen protection, is however different from the prior art. Therefore, present claim 1 appears to meet the requirements of Article 33(2)(3) PCT. The same holds true for present claim 2 and for dependent claims 3 - 5, 8 and 9 as well as for present claim 12 directed to the use of salicylic

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/04141

acid in combination with over expression of BiP to protect a plant against pathogen attack.

2.2 Present claim 6 is directed to a method of reducing the period within which a plant's natural defence mechanism responds to pathogen attack by over expression of calreticulin. It is not apparent from the description that over expression of calreticulin would solve the technical problem, i.e. reducing the period within which a plant's natural defence mechanism responds to pathogen attack. The claim therefore does not meet the requirements of Article 33(3) EPC. The same holds true for present claims 7 and 9.

2.3 The applicant is requested to note that vague statements like "... the maintained level (of BiP) may be affected by over expression of calreticulin ..." or "high levels of calreticulin will induce high levels of BiP" (page 5, lines 28-32) are not suitable for establishing an effect that would solve the technical problem. Moreover, Examples 1 (page 14, lines 32-34) and 7 (page 18, lines 26-28) only demonstrate that enhanced BiP levels are coinciding with enhanced levels of calreticulin. The examples do not show that over expression of calreticulin leads to enhanced levels of BiP.

2.4 Present claims 10, 11, 13 and 14 are directed to plants or plant cells with a level of BiP that is three or five times higher compared to the level in unmodified plants. Documents D1 (page 816, right-hand column, last two lines) and D2 (page 7095, right-hand column, last paragraph) disclose transgenic plants with increased BiP levels. D1 and D2 do, however, not disclose the level of overexpression. Nevertheless, the IPEA is of the opinion that the term "over expression" implies a level that is clearly elevated compared to a non-modified plant, i.e. levels that are three - five times higher. The subject-matter of claims 10, 11, 13 and 14 is thus anticipated by D1 and D2. The claims do not meet the requirements of Article 33(2) PCT.

2.5 Even if the applicant would succeed in establishing formal novelty the claims would still not meet the requirements of Article 33(3) PCT. Enhanced expression levels have always been a primary goal in plant biotechnology. A man skilled in the art is aware of various possibilities (promoters, introns, ...) to reach that goal.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/04141

and would apply them according to his needs.

Re Item VIII

Certain observations on the international application

1. Present claim 1 is lacking an essential technical feature. It is clear from the description (Examples 5, 12 and page 26, first paragraph) that the only way to increase the level of luminal binding protein (BiP) in a plant, that was put into practice by the applicant, is to transform that plant with a gene encoding BLP4. Since independent claim 1 does not contain this feature it does not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention. The same holds true for dependent claims 2 - 4, 8 and 9.
2. Present claims 6 and 7 do not meet the requirements of Article 5 PCT. It is not apparent from the description that the over expression of calreticulin and the ATPase domain of BiP would lead to an enhanced level of BiP in a plant.
3. The term "strong constitutive promoter" in present claims 6, and 7 does not constitute a definition in terms of technical features as required by Rule 6.3(a) PCT. The claims are thus considered unclear (Article 6 PCT).

Amended Claims

1. A method of increasing the capacity for secretory protein synthesis in general (i.e. not restricted to PR genes), the method comprising causing a plant to maintain in
5 at least a part of the plant a level of BiP, or a homologue thereof, which is greater than the endogenous level for said plant in non-stressful conditions.
2. A method according to claim 1 of reducing the period within which the plant's natural defence mechanism responds to attack by a plant pathogen.
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3. A method according to either claim 1 or 2 wherein the maintained level of BiP, or a homologue thereof, is at least three times said endogenous level.
4. A method according to claim 3 wherein said maintained level is at least five
15 times said endogenous level.
5. A method according to any preceding claim wherein said maintained level is effected by over expression of BiP, or a homologue thereof, by means of a chimeric gene containing a strong constitutive promoter, a coding region for BiP or a
20 homologue thereof and a 3' untranslated end containing a stop sequence.
6. A method according to any of claims 1 to 4 wherein said maintained level is effected by over expression of calreticulin, or a homologue thereof, by means of a chimeric gene containing a strong constitutive promoter, a coding region for
25 calreticulin or a homologue thereof and a 3' untranslated end containing a stop sequence.
7. A method according to any of claims 1 to 4 wherein said maintained level is effected by over expression of the ATPase domain of BiP, or a homologue thereof,
30 and an ER retention signal by means of a chimeric gene containing a strong constitutive promoter, a coding region for the ATPase domain of BiP, or a homologue thereof, and for an ER retention signal and a 3' untranslated end containing a stop sequence.
- 35 8. A method according to any of claims 1 to 4 wherein said maintained level is effected by modifying signal transduction pathways leading to BiP induction.

9. A method according to any of the preceding claims wherein the plant is additionally treated with salicylic acid.
10. A modified plant which maintains, in at least a part thereof, a level of BiP, or a homologue thereof, of at least a three times greater than the level maintained in said part by an unmodified plant of the same species in non-stressful conditions.
11. A modified plant according to claim 10 wherein the BiP level is at least five times greater than the level maintained by an unmodified plant of the same species in non-stressful conditions.
12. Use of salicylic acid in combination with over expression of BiP or a homologue thereof to protect a plant against pathogen attack.
13. A modified plant or plant cells with a level of BiP, or a homologue thereof, which is at least three times greater than the endogenous level of the plant or plant cells in non-stressful conditions, produced by the method of the present invention.
14. A modified plant or plant cells according to claim 13 wherein the BiP level is at least five times greater than the endogenous level of the plant or plant cells in non-stressful conditions.

P15578woamendedclaims

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference LPB/P15578W0	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 99/ 04141	International filing date (day/month/year) 14/12/1999	(Earliest) Priority Date (day/month/year) 15/12/1998
Applicant THE UNIVERSITY OF YORK et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☒ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

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☐ None of the figures.

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims : 1 and 11 completely, and 3-10, 12 all partially
Method for reducing the period within which a plant's natural defense mechanism responds to pathogen attack
2. Claims : 2 completely and 3-10, 12 all partially
A method for increasing secretory protein synthesis capacity in plants

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12N15/82 C12N5/10 A01H5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>CROFTS ANDREW J ET AL: "BiP and calreticulin form an abundant complex that is independent of endoplasmic reticulum stress." PLANT CELL, vol. 10, no. 5, May 1998 (1998-05), pages 813-823, XP002137296 ISSN: 1040-4651 page 816, right-hand column -page 818, left-hand column</p> <p style="text-align: center;">--- -/--</p>	10,12

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

10 May 2000

Date of mailing of the international search report

23/05/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Maddox, A

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	COLEMAN CRAIG E ET AL: "Expression of a mutant alpha-zein creates the floury2 phenotype in transgenic maize." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 1997, vol. 94, no. 13, 1997, pages 7094-7097, XP002137297 ISSN: 0027-8424 page 7095, right-hand column ---	10,12
P,X	LEBORGNE-CASTEL NATHALIE ET AL: "Overexpression of BiP in tobacco alleviates endoplasmic reticulum stress." PLANT CELL , vol. 11, no. 3, March 1999 (1999-03), pages 459-469, XP002137298 ISSN: 1040-4651 the whole document ---	2-5,7, 10,12
P,X	JELITTO-VAN DOOREN EDITH P W M ET AL: "Anticipating endoplasmic reticulum stress: A novel early response before pathogenesis-related gene induction." PLANT CELL, vol. 11, no. 10, October 1999 (1999-10), pages 1935-1943, XP002137299 ISSN: 1040-4651 the whole document ---	1,3-5,7, 10,12
P,A	CROFTS ANDREW J ET AL: "Saturation of the endoplasmic reticulum retention machinery reveals anterograde bulk flow." PLANT CELL NOV., 1999, vol. 11, no. 11, November 1999 (1999-11), pages 2233-2247, XP002137300 ISSN: 1040-4651 page 2237, right-hand column -page 2238L ---	6
A	DENECKE JURGEN ET AL: "The Tobacco Homolog of Mammalian Calreticulin Is Present in Protein Complexes in Vivo." PLANT CELL 1995, vol. 7, no. 4, 1995, pages 391-406, XP002137301 ISSN: 1040-4651 page 399, right-hand column -page 400 --- -/--	1

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>VIDAL SABINA ET AL: "Salicylic acid and the plant pathogen Erwinia carotovora induce defense genes via antagonistic pathways." PLANT JOURNAL 1997, vol. 11, no. 1, 1997, pages 115-123, XP002137302 ISSN: 0960-7412 the whole document</p>	1
A	<p>--- DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, USJanuary 1998 (1998-01) VIDAL SABINA ET AL: "Cell wall-degrading enzymes from Erwinia carotovora cooperate in the salicylic acid-independent induction of a plant defense response." Database accession no. PREV199800083794 XP002137308 abstract & MOLECULAR PLANT-MICROBE INTERACTIONS JAN., 1998, vol. 11, no. 1, January 1998 (1998-01), pages 23-32, ISSN: 0894-0282</p>	1
A	<p>--- MORRIS JILL A ET AL: "Immunoglobulin binding protein (BiP) function is required to protect cells from endoplasmic reticulum stress but is not required for the secretion of selective proteins." JOURNAL OF BIOLOGICAL CHEMISTRY 1997, vol. 272, no. 7, 1997, pages 4327-4334, XP002137303 ISSN: 0021-9258 the whole document</p>	2
A	<p>--- ROBINSON ANNE SKAJA ET AL: "Reduction of BiP levels decreases heterologous protein secretion in Saccharomyces cerevisiae." JOURNAL OF BIOLOGICAL CHEMISTRY 1996, vol. 271, no. 17, 1996, pages 10017-10022, XP002137304 ISSN: 0021-9258 the whole document</p>	2
A	<p>--- WO 94 08012 A (RES CORP TECHNOLOGIES INC) 14 April 1994 (1994-04-14) the whole document</p> <p style="text-align: center;">--- -/--</p>	2

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HARMSSEN M M ET AL: "OVEREXPRESSION OF BINDING PROTEIN AND DISRUPTION OF THE PMR1 GENE SYNERGISTICALLY STIMULATE SECRETION OF BOVINE PROCHYMOSIN BUT NOT PLANT THAUMATIN IN YEAST" APPLIED MICROBIOLOGY AND BIOTECHNOLOGY, DE, SPRINGER VERLAG, BERLIN, vol. 46, no. 4, 1996, pages 365-370, XP002045333 ISSN: 0175-7598 the whole document	2
A	WO 98 21346 A (KO KENTON ; PANG PENG (CA); UNIV KINGSTON (CA)) 22 May 1998 (1998-05-22) the whole document	2
A	DENECKE J ET AL: "THE TOBACCO LUMINAL BINDING PROTEIN IS ENCODED BY A MULTIGENE FAMILY" PLANT CELL 1991, vol. 3, no. 9, 1991, pages 1025-1036, XP002137305 ISSN: 1040-4651 the whole document	1-12

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

GB 99/04141

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9408012	A	14-04-1994	EP	0663010 A	19-07-1995
			US	5773245 A	30-06-1998
WO 9821346	A	22-05-1998	US	5919999 A	06-07-1999
			AU	4858197 A	03-06-1998
			EP	0941348 A	15-09-1999

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

11 August 2000 (11.08.00)

International application No.

PCT/GB99/04141

Applicant's or agent's file reference

LPB/P15578WO

International filing date (day/month/year)

14 December 1999 (14.12.99)

Priority date (day/month/year)

15 December 1998 (15.12.98)

Applicant

DENECKE, Jurgen et al

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

12 July 2000 (12.07.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Pascal Piriou

Telephone No.: (41-22) 338.83.38

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

HARRISON GODDARD FOOTE
Tower House
Merrion Way
Leeds LS6 8PA
ROYAUME-UNI

Date of mailing (day/month/year)

27 July 2000 (27.07.00)

Applicant's or agent's file reference

LPB/P15578WO

IMPORTANT NOTIFICATION

International application No.

PCT/GB99/04141

International filing date (day/month/year)

14 December 1999 (14.12.99)

1. The following indications appeared on record concerning:

☐

the applicant

☐

the inventor

☒

the agent

☐

the common representative

Name and Address

HARRISON GODDARD FOOTE
Belmont House
20 Wood Lane
Leeds LS6 2AE
United Kingdom

State of Nationality

State of Residence

Telephone No.

44-113-225-8350

Facsimile No.

44-113-230-4702

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐

the person

☐

the name

☒

the address

☐

the nationality

☐

the residence

Name and Address

HARRISON GODDARD FOOTE
Tower House
Merrion Way
Leeds LS6 8PA
United Kingdom

State of Nationality

State of Residence

Telephone No.

44-113-290 1400

Facsimile No.

44-113-244 2829

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒

the receiving Office

☒

the designated Offices concerned

☐

the International Searching Authority

☐

the elected Offices concerned

☐

the International Preliminary Examining Authority

☐

other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Ingrid Aulich

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

MAGGS, Michael, Norman
Kilburn & Strode
20 Red Lion Street
London WC1R 4PJ
ROYAUME-UNI

TECHCENTER 1600/2800

FEB 19 2002

RECEIVED

Date of mailing (day/month/year) 21 August 2001 (21.08.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference MNM/P21301WO	
International application No. PCT/GB99/04318	International filing date (day/month/year) 17 December 1999 (17.12.99)

1. The following indications appeared on record concerning:

☒ the applicant ☒ the inventor ☐ the agent ☐ the common representative

Name and Address DOLL-STEINBERG, Daniel 5 Bendall Mews Marylebone London NW1 6SN United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address DOLL-STEINBERG, Daniel 126/134 Baker Street London W1U 6UE United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned
☐ the International Searching Authority ☒ the elected Offices concerned
☒ the International Preliminary Examining Authority ☐ other:


The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer CORTIELLO Maria Victoria Telephone No.: (41-22) 338.83.38
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11 APR 2001

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference LPB/P15578WO		FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB99/04141	International filing date (day/month/year) 14/12/1999	Priority date (day/month/year) 15/12/1998		
International Patent Classification (IPC) or national classification and IPC C12N15/82				
Applicant THE UNIVERSITY OF YORK et al.				
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 2 sheets.</p>				
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application 				
Date of submission of the demand 12/07/2000		Date of completion of this report 05.04.2001		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Burkhardt, P Telephone No. +49 89 2399 7456		



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/04141

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-32 as originally filed

Claims, No.:

1-14 with telefax of 22/12/2000

Drawings, sheets:

1/17-17/17 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/04141

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1 - 9, 12
	No:	Claims	10, 11, 13, 14
Inventive step (IS)	Yes:	Claims	1 - 5, 8, 9, 12
	No:	Claims	6, 7
Industrial applicability (IA)	Yes:	Claims	1 - 14
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item I

Basis of the opinion

The amended claims filed with the letter of 22.12.2000 are formally acceptable under Article 34(2)(b) PCT.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following documents (D) are referred to in this report; the numbering is following the order of the International Search Report:

- D1 Crofts *et al.*, 1998. Plant Cell 10:813-823.
- D2 Coleman *et al.*, 1997. PNAS USA 94:7094-7097.

1. Interpretation of claims

1.1 In order to allow a meaningful examination of the present set of claims it was assumed that the methods relate to transgenic plants that have been transformed with a nucleic acid sequence encoding a luminal binding protein (BiP).

1.2 Please also note the comments in section VIII.

2. Article 33(2)(3) PCT (Novelty and inventive step)

2.1 Present claim 1 is directed to a method of reducing the period within which a plant's natural defence mechanism responds to pathogen attack by over expression of BiP. The transgenic plants disclosed in D1 and D2 have been created in the same way as those of the present invention. The result to be achieved, namely to obtain an improved pathogen protection, is however different from the prior art. Therefore, present claim 1 appears to meet the requirements of Article 33(2)(3) PCT. The same holds true for present claim 2 and for dependent claims 3 - 5, 8 and 9 as well as for present claim 12 directed to the use of salicylic

acid in combination with over expression of BiP to protect a plant against pathogen attack.

2.2 Present claim 6 is directed to a method of reducing the period within which a plant's natural defence mechanism responds to pathogen attack by over expression of calreticulin. It is not apparent from the description that over expression of calreticulin would solve the technical problem, i.e. reducing the period within which a plant's natural defence mechanism responds to pathogen attack. The claim therefore does not meet the requirements of Article 33(3) EPC. The same holds true for present claims 7 and 9.

2.3 The applicant is requested to note that vague statements like "... the maintained level (of BiP) may be affected by over expression of calreticulin ..." or "high levels of calreticulin will induce high levels of BiP" (page 5, lines 28-32) are not suitable for establishing an effect that would solve the technical problem. Moreover, Examples 1 (page 14, lines 32-34) and 7 (page 18, lines 26-28) only demonstrate that enhanced BiP levels are coinciding with enhanced levels of calreticulin. The examples do not show that over expression of calreticulin leads to enhanced levels of BiP

2.4 Present claims 10, 11, 13 and 14 are directed to plants or plant cells with a level of BiP that is three or five times higher compared to the level in unmodified plants. Documents D1 (page 816, right-hand column, last two lines) and D2 (page 7095, right-hand column, last paragraph) disclose transgenic plants with increased BiP levels. D1 and D2 do, however, not disclose the level of overexpression. Nevertheless, the IPEA is of the opinion that the term "over expression" implies a level that is clearly elevated compared to a non-modified plant, i.e. levels that are three - five times higher. The subject-matter of claims 10, 11, 13 and 14 is thus anticipated by D1 and D2. The claims do not meet the requirements of Article 33(2) PCT.

2.5 Even if the applicant would succeed in establishing formal novelty the claims would still not meet the requirements of Article 33(3) PCT. Enhanced expression levels have always been a primary goal in plant biotechnology. A man skilled in the art is aware of various possibilities (promoters, introns, ...) to reach that goal

and would apply them according to his needs.

Re Item VIII

Certain observations on the international application

1. Present claim 1 is lacking an essential technical feature. It is clear from the description (Examples 5, 12 and page 26, first paragraph) that the only way to increase the level of luminal binding protein (BiP) in a plant, that was put into practice by the applicant, is to transform that plant with a gene encoding BLP4. Since independent claim 1 does not contain this feature it does not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention. The same holds true for dependent claims 2 - 4, 8 and 9.
2. Present claims 6 and 7 do not meet the requirements of Article 5 PCT. It is not apparent from the description that the over expression of calreticulin and the ATPase domain of BiP would lead to an enhanced level of BiP in a plant.
3. The term "strong constitutive promoter" in present claims 6, and 7 does not constitute a definition in terms of technical features as required by Rule 6.3(a) PCT. The claims are thus considered unclear (Article 6 PCT).